Book Reviews

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Molecular Variants in Disease (Symposium organized by The Royal College of Pathologists delivered in London in February 1974). Edited by D. N. Raine. (Pp. 166; illustrated. £3.00.) Published for The Royal College of Pathologists by the *Journal of Clinical Pathology*, B.M.A. House, London. 1974.

Elucidation of the primary enzyme or protein abnormality of many inherited disorders has been achieved in the past 10 years and this useful book contains a selection of these studies. There are detailed accounts of the mucopolysaccharidoses, lipidoses, and glycogen storage disorders. The Lesch-Nyhan syndrome and other disorders of purine metabolism are reviewed and there is an interesting account of vitamin-responsive genetic disease. Haemoglobinopathies and erythrocyte enzyme deficiencies are also considered in some detail. Though the biochemical features of inherited disorders are emphasized, clinical summaries, including treatment and prenatal diagnosis, are also provided.

Knowledge of the primary enzyme defect has led to the recognition that variant forms of inherited diseases are not uncommon and the title of this book reflects current interest in this field. Many examples of molecular variants are to be found throughout the text, and the theoretical basis for their occurrence is given in a valuable article on genetic heterogeneity in inherited diseases. This contains a vivid illustration of the large number of variants of a polypeptide to be expected. It is estimated that more than 800 variants of the haemoglobin β chain could be generated by single base-change mutations in the β Hb gene. Almost 300 would differ in charge from the normal molecule and so could be detected by electrophoresis and then checked by amino acid sequencing; at least 60 of these variants have already been described. There is no reason to think that the haemoglobin β gene locus is in any way peculiar and many more variant forms of other important proteins will no doubt be found.

A related theme which can be picked out from the articles on individual disorders is the realization that only one component form or one isozyme of a total enzyme activity might be deficient or defective in a particular disorder. A short article on isozymes is, therefore, helpful in drawing attention to the various ways in which they can be formed.

Screening an apparently healthy population for metabolic disorders raises many problems. These are thoughtfully considered and the importance of having a clear idea of the purpose of a screening programme is stressed. In the concluding article, the need for a

national policy for the management of inherited disease is suggested. But the complex organization proposed will have to be carefully examined to determine whether its cost can be justified by improvements in diagnosis and treatment. The circulation of a register of centres that are able to provide information and help to paediatricians dealing with suspected cases of inherited disorders might be a cheaper though adequate alternative at present.

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Mendelian Inheritance in Man: Catalogs of Autosomal Dominant, Autosomal Recessive and X-Linked Phenotypes, 4th ed. By Victor A. McKusick. (Pp. lxxx+837; £9.60.) London and Baltimore: The Johns Hopkins University Press. 1975.

Dr McKusick's continually revised catalogue of Mendelising phenotypes in the human is familiar to practising medical geneticists and has come to be relied upon for its comprehensiveness. It is pleasing to see in this edition that the computer which stores information for these catalogues is able not only to memorize but also to learn! It has been taught to use lower case characters as well as capitals and this, coupled with the use of thinner paper, has kept the book to the same size as before in spite of much new information.

For each phenotype listed in the dominant (autosomal), recessive (autosomal), and X-linked catalogues there is first a short account of the phenotype and then a resumé of relevant genetic information and finally a list of key references. The entries are numbered and each number is intended permanently to represent a gene locus. Some phenotypes have been fragmented by the 'splitters' who have sought and found heterogeneity while others are beginning to coalesce as the new 'lumpers' find possible examples of loci common to diverse phenotypes (e.g. the Scheie syndrome which has lost its asterisk in favour of the Hurler locus). Phenotypes with an asterisk are those for which the mode of inheritance is certain while those without an asterisk are entered heuristically, a procedure which is justified by the hundred or so entries which have earned asterisks since the last edition.

Genetics reference books of this kind are often made less useful by a poor index but in *Mendelian Inheritance in Man* the index is thorough and very useful. The subject index has not only the preferred and alternative names for the phenotypes but also their major clinical features, and the author index has 14 000 names.